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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,859	09/02/1999	JAMES SAMSOONDAR	5352-051	4860

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EXAMINER	
SODERQUIST, ARLEN	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 01/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/367,859	SAMSOONDAR, JAMES	
	Examiner	Art Unit	
	Arlen Soderquist	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,10-12,23,24,27,29,30,34 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,10-12,23,24,27,29,30,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. If applicant desires priority under 35 U.S.C. 365(c) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 8, 10-12, 23-24, 27, 29-30 and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis in view of Sagusa, Gimpel, Simon and Christenson, Leissing or Mullins. In the patent Davis teaches a method of detecting hemolysis in a whole-blood sample, a method of determining an elevation in the potassium ion concentration of a whole-blood sample, an apparatus for detecting hemolysis and/or determining an elevation in the potassium ion concentration in a fluid sample, an apparatus for detecting hemolysis and/or determining an elevation in the potassium ion concentration in a whole-blood sample, and a single-use cartridge containing a plurality of microfabricated biosensors which further contains a hemolysis detection unit. Thus Davis separately detects the presence of hemoglobin in the blood sample consistent with the prior art as taught in column2, lines 46-52. Columns 2-3 of the application teach the interference from hemoglobin caused through hemolysis of red blood cells through both an increase in the concentration of other components found in the red blood cells or through colorimetric interference with chromogenic reagents. In particular the above noted column 2, lines 46-52 teaches the prior method of checking the color of the plasma sample for the red coloration associated with the presence of hemolysis. Column 3, lines 12-18 list several analytes which can be affected through the presence of hemolysis including potassium, lactate

dehydrogenase, cholesterol, prostatic phosphatase, aspartate aminotransferase, and alanine aminotransferase, aldolase, total acid phosphatase, isocitrate hydrogenase, magnesium and phosphate. Columns 6-8 teach how the presence of hemoglobin is detected with column 8 lines, 10-36 being particularly relevant to the instant claims. This section of column 8 teaches the use of a reflectance meter, the use of a direct measurement (no chromogenic reagent is used) and forming a calibration graph to determine the concentration of hemoglobin present. Columns 8-9 teach how the measurement of the hemoglobin concentration is used to correct the analyte measurement. Of particular interest is column 9, lines 44-56 teaching the relationships between hemolyzed red blood cells, the concentration of Hb, and the elevation of blood analytes such as potassium ion concentration. The relationship for potassium is taught as a linearly dependent relationship. As a result, those of ordinary skill in the art will be able to pre-select a value of hemolysis which corresponds to both a known concentration of Hb in plasma and the corresponding color thereof, which in turn correlates to a pre-selected elevation in the potassium ion concentration. Davis does not teach interference by blood substitutes or other components of the blood, using derivative spectroscopy in the correction equation or detection of pseudohemolysis.

In the patent Sagusa teaches a colorimetric method for samples including interfering chromogens from the presence of chyle, hemolysis and icterus. Column 3 discusses how these things interfere with the analysis of the analytes. Color former is added to blood serum sample color it, and measurements for specific components are determined based on the light absorbance caused by coloring. For one sample, a differential light absorbance between two wavelengths at each of long wavelength region, middle wavelength region and short wavelength region within a visible wavelength band is determined. The degree of chyle is determined from the measurements for the long wavelength region, the degree of hemolysis is determined from the measurements for the middle wavelength region, and the degree of icterus is determined from the measurements for the short wavelength region. The measurements for the specific components are then corrected by the degree of chyle, degree of hemolysis and degree of icterus to obtain highly correct measurements. Column 4 shows some example wavelengths and columns 4-5 show how the degree of chyle, hemolysis and icterus are obtained and used to correct the analyte concentration. In this discussion equation (4) is particularly important because it shows that the

relationship between each of the degree of chyle, hemolysis and icterus and the respective analytes are linear depending only on a constant and the concentration representative of the degree of chyle, hemolysis and icterus.

In the abstract Christenson discusses hemoglobin based blood substitutes and their interference with routine chemical tests.

In the abstract Leissing discusses modification of clinical chemistry methods to overcome interferences from diaspirin crosslinked hemoglobin (DCLHb).

In the paper Mullins discusses effects of Fluosol-DA (artificial blood) on clinical chemistry tests and instruments. Artificial blood must be added to the list of therapeutic agents that produce interference with diagnostic laboratory tests. Fluosol-DA (Alpha Therapeutic Corp., Los Angeles, CA), a stable 20% emulsion of perfluorocarbons in aqueous medium, is being evaluated in clinical trials as a blood substitute in the United States. They investigated its effects in blood and serum samples on test results and instruments in the clinical chemistry laboratory. The 20% emulsion was added to blood or serum specimens in amounts corresponding to the replacement of in-vivo plasma volumes of 10-50%, concentrations that would be expected in blood samples obtained from patients who have received Fluosol. Observed interferences mimicked those caused by high triglyceride concentrations in serum specimens: interference with chemical reactions and generation of spurious absorbance readings because of turbidity. These types of errors are often additive, and the cumulative effect may cause either erroneously high or low values for the analytes concerned. Because Fluosol may be used widely, although infrequently, for patients refusing blood transfusions on religious grounds and for patients with rare antibodies to red blood cells who require transfusion, laboratories analyzing specimens containing Fluosol should be aware of the potential errors.

In the paper Gimpel teaches a reference interval for the bilirubin excess in cerebrospinal fluid by derivative spectrophotometry. The value of the bilirubin excess can be a useful aid for recognizing blood from hemorrhage in cerebrospinal fluid. One of the parameters needed for the calculation of the bilirubin excess is the total bilirubin concentration in cerebrospinal fluid. A method for measuring total bilirubin in cerebrospinal fluid is presented, based on diazotization of bilirubin according to Jendrassik-Grof, combined with multiwavelength first-derivative spectrophotometry. This bilirubin assay allows determination of total bilirubin concentrations as

low as 0.045 μmol/L. This method also enables a correlation for oxyHb interference. The value of the bilirubin excess was calculated for patients not showing any neurological disorder. A reference interval of 0.07 ± 0.06 μmol/L was calculated for the bilirubin excess. Particularly relevant to the instant claims is the calculations and equations shown in the right column of page 218.

In the paper Simon discusses a "pseudo-hemolytic" transfusion reaction caused by intravenous iron-dextran therapy. Intravenous iron-dextran therapy can cause a red-brown discoloration of the plasma, simulating a hemolytic transfusion reaction. A rapid and simple test to differentiate between true hemolysis and plasma discoloration due to circulating iron-dextran complexes is described.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes recognized by Christenson, Leissing or Mullins as interfering substances and other known interfering ssubstances such as those taught by Sagusa into the Davis correction method because of the recognized possibility for interference with clinical chemistry tests and the projected use of these substances in humans. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use different wavelengths as taught in the Sagusa method to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as taught by Simon and Sagusa in the Davis method because of the ability to select wavelengths that will allow the effects of one chromogen to be removed from another chromogen as taught by Sagusa and the need to differentiate between true hemolysis and plasma discoloration due to circulating substances as taught by Simon. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative spectroscopic method as shown by Gimpel for correction in the Davis method because of the ability to differentiate between interfering substances such as the hemoglobin and bilirubin of Gimpel. Determination of specific wavelengths would be a results effective variable which has been held to be within the skill of the routineer in the art by the Courts (see *In re Boesch*, 205 USPQ 215 (CCPA 1980)).

4. Applicant's arguments filed November 15, 2004 have been fully considered but they are not persuasive. Examiner agrees that none of the references anticipate the claims. However,

examiner believes that the combination of references does meet and show the obviousness of the instant claims. The Davis reference clearly deals with correction of analyses in the presence of an interfering substance such as hemoglobin from hemolysis of a blood sample and it separates the detection of the interfering substance from the detection of the analyte. Davis also clearly teaches the detection of the hemoglobin from hemolysis in the absence of a chromogenic reagent (column 8, lines 18-36). Relative to claim 8, the relationship in Davis between the hemoglobin concentration and the potassium concentration is linear. This same relationship exists in Sagusa between each of the interfering substances and the analyte being measured. Thus the use of a linear relationship would have been expected for the relationship with at least the interfering substances taught by Sagusa particularly in view of the fact that hemoglobin, the interfering substance of Davis, is one of the interfering substances taught in Sagusa. Sagusa also clearly shows that one of skill in the art would have recognized that other things interfere with the analysis of components of blood and therefore would have motivated one of skill in the art to include other potential interferon's into the correction process. Relative to claim 24, the claim does not explicitly require a classification or determination step and examiner is treating them as the detection of hemoglobin or a blood substitute constitutes the determination. The Davis reference recognizes that the presence of an interfering substance can affect the results (interfere) in two ways: increasing the concentration of a measured component from is release from the red blood cells through hemolysis and through interfering with the color formed in the analysis. The Sagusa reference shows that one of skill in the art also recognizes that interferences can interfere by overlapping the spectrum used to measure the analyte (the second method taught by Davis). Thus when the Christenson, Leissing or Mullins references teach that blood substitutes also interfere with the analysis of analytes, it would have been obvious to include them into the process for correcting the concentration of known interfering substances to overcome the known affects of an interfering compound as shown by both Davis and Sagusa. The presence of substances in the blood (blood substitutes) that would also interfere with an analysis in a manner similar to hemolysis is shown by the secondary references as well as means to remove the influence of the interfering compounds. Thus it would have been obvious to modify the teachings of Davis to include the possibility of pseudohemolysis due to its recognized presence and effects on the analysis of other components of a blood sample. Since the references are

dealing with interfering substances in an analysis they are properly combinable. The Courts have recognized that a secondary reference does not need to be physically combinable with the primary reference to render the invention under review obvious. Along these lines applicant is directed to *In re* Sneed 218 USPQ 385, 389 (Fed. Cir. 1983) and *In re* Keller 208 USPQ 871, 880 (CCPA 1981) . Relative to the use of derivative spectroscopy, it is noted that the limitation is not currently in the claims as an explicitly stated limitation. The Gimpel reference is included because of previous claims that explicitly included such limitations and the possibility that the limitations are implied by the linear relationship required in the instant claims. The Gimpel reference shows that derivative spectroscopy is a way of obtaining a measurement of substances such as bilirubin, a known interfering substance in blood analyses. The reference also deals with the removal of influences due to interfering compounds. Thus, Gimpel shows that the use of derivative spectroscopy is a way of measuring the presence of one or more components of a blood sample and would have motivated one of skill in the art to use the technique for appropriate components of the blood sample.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose current telephone number is (571) 272-1265. The examiner's schedule is variable between the hours of about 6:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Arlen Soderquist

January 3, 2005

ARLEN SODERQUIST
PRIMARY EXAMINER